

NEUROTENSIN AND THE BLOOD BRAIN BARRIER

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Neurotensin is an endogenous tridecapeptide that was first isolated and characterized twenty years ago. With a distribution that includes gut neurons as well as such regions as the hypothalamus and many other central nervous system sites, neurotensin still does not have a well defined physiological role that integrates both brain and gut actions. Brain NT systems seem to be closely associated with dopamine systems, NT is co-localized within a sub-population of dopamine neurons and is enriched in concentration in brain regions containing dopamine terminals. Direct injection of NT into the brain causes hypothermia, potentiation of the sedative effects of depressant drugs and opposes the effects of dopamine agonists without blockade of dopamine receptors. These actions led to the hypothesis that NT is an endogenous neuroleptic-like compound and decreased levels of NT were subsequently detected in spinal fluid of schizophrenics and clinically effective neuroleptic drugs were shown to increase NT concentrations specific brain regions in laboratory animals. Because none of these effects are seen after peripheral NT administration, the acid test of the endogenous neuroleptic hypothesis, which would be clinical antipsychotic trials of NT, have not been feasible. Recently, NT analogs that potentiate pentobarbital sedation and produce hypothermia after intraperitoneal injection have been synthesized. These preliminary data will be presented and indicate that clinical trials of NT as an antipsychotic may be imminent.